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13. ABSTRACT *(Maximum 200 words)*

As in the prior material, the largest population of neurons in the Human SCN contains NT. These are distributed throughout the nucleus and are accompanied by a dense axonal plexus which is probably intrinsic. The NT plexus is uniformly dense throughout the SCN with numerous, small varicosities. These are distributed in a pattern that indicates the synapses are predominantly axodendritic. The second largest population of neurons is VP - containing. These also are widely distributed but perikarya are not present in the ventral-medial portion of the nucleus. The VP plexus is also dense and the distribution of axons also indicates a predominantly axodendritic synapse organization. NPY - containing neurons are found predominantly in the central part of the SCN. There is a dense, and quite coarse, plexus of varicosities and axons peripherally with many fewer axons in the area of NPY cell bodies. The plexus includes a set of very fine fibers and varicosities that presumably arise either from the SCN neurons or the lateral geniculate. VIP perikarya are located very ventrally and medially in the nucleus. Axons project through the nucleus and out into the adjacent anterior hypothalamus. The area innervated by these VIP fivers appears much wider than in therat and includes the paraventricular nucleus.

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AIR FORCE OFFICE OF SCIENTIFIC RESEARCH

ANNUAL TECHNICAL REPORT

"ORGANIZATION OF THE HUMAN-CIRCADIAN SYSTEM"

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Project Period: 2/1/91 - 1/31/92

TECHNICAL REPORT

Objectives. The overall objective of this project is to provide a detailed description of the organization of the primate, particularly human, circadian timing system. The specific objectives for this project year were as follows: 1) Immunohistochemical analysis of the human SCN; 2) Immunohistochemical analysis of the monkey SCN: 3) Analysis o f retinal projections to the hypothalamus and lateral geniculate in the macaque monkey.

Status of the Research Effort. This will be described for each of the objectives noted above. During the last year we have received an additional 6 human hypothalami and did one additional monkey with cholera toxin injection into the eye. Two of the human hypothalami were obtained with a short postmortem interval. This did not affect most of the immunohistochemical staining but did result in greatly improved staining for vasoactive intestinal polypeptide (VIP).

Human SCN - Immunohistochemical Analysis. As for the last report, the human hypothalamic obtained this year were from quite varied aged individuals, both male and female. Most of the tissue was stained with antisera to VIP, vasopressin (VP), neurotensin (NT) and neuropeptide Y (NPY). As in the prior material, the largest population of neurons in the SCN contains NT. These are distributed throughout the nucleus and are accompanied by a dense axonal plexus which is probably intrinsic. The NT plexus is uniformly dense throughout the SCN with numerous, small varicosities. These are distributed in a pattern that indicates the synapses are predominantly axodendritic. The second largest population of neurons is VP- containing. These also are widely distributed but perikarya are not present in the ventral-medial portion of the nucleus. The VP plexus is also dense and the distribution of axons also indicates a predominantly axodendritic synapse organization. NPY- containing neurons are found predominantly in the central part of the SCN. There is a dense, and quite coarse, plexus of varicosities and axons

peripherally with many fewer axons in the area of NPY cell bodies. The plexus includes a set of very fine fibers and varicosities that presumably arise either from the SCN neurons or the lateral geniculate. VIP perikarya are located very ventrally and medially in the nucleus. Axons project through the nucleus and out into the adjacent anterior hypothalamus. The area innervated by these VIP fibers appears much wider than in the rat and includes the paraventricular nucleus.

Monkey SCN - Immunohistochemical Analysis. The monkey SCN lies adjacent to the optic chiasm and medial to the third ventricle. It is separated from the third ventricle by a thin periventricular nucleus. As in the human, the monkey SCN contains VP-, VIP- and NT - containing neurons. The VIP neurons essentially overlap the zone of major termination of the retinohypothalamic tract in the SCN. There is a dense VIP plexus that extends beyond the cell region into the zone occupied by VP neurons. The VP plexus extends from the supraoptic nucleus to the paraventricular nucleus. It, too, is quite dense. There are very few NTR neurons in the monkey SCN, and very sparse plexus, in contrast to the human. No immunoreactive NPY neurons are present in the monkey. Rather, there is only a plexus that overlaps the zone of retinal afferents.

Retinal Projections to the Lateral Geniculate and Hypothalamus in the Monkey. Retinal projections to the lateral geniculate, particularly the perigeniculate nucleus, were assessed using material in which cholera toxin was injected into one eye. The perigeniculate nucleus lies largely dorsal and medial to the dorsal lateral geniculate. It is cytoarchitectonically homogeneous but should consist of intergeniculate leaflet (IGL) and ventral lateral geniculate (VLG). The projection to the IGL should be bilateral whereas that to VLG should be predominantly bilateral. On this basis, it appears that the VLG homologue in the monkey is the dorsal component of the perigeniculate complex. This receives a predominantly contralateral projection as would be expected for VLG. The medial part of the nucleus receives a bilateral projection, greater to the

contralateral than ipsilateral side. In the current year, we have injected another monkey and harvested the brain but the material has not yet been processed. To do this we will use an antiserum to cholera toxin to analyze the retinal projections. In rat material, this is more sensitive than the cholera toxin - HRP method. In addition, this will permit us to do standard peptide immunohistochemistry on the material, something not possible with the other method. It will also provide a more detailed analysis of retinohypothalamic projections.

Publications:

1. Moore, R.Y. Organization of the human circadian system. Progress in Brain Research, in press.

2. Moore, R.Y. and Speh, J.C. Retinohypothalamic projections and the organization of the Suprachiasmatic nucleus in the macaque monkey. In preparation. To be submitted to the Journal for Neuroscience.

3. Moore, R.Y. and Speh, J.C. Intergeniculate leaflet and ventral lateral geniculate nucleus in the macaque monkey. In preparation. To be submitted to Visual Neuroscience.

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Papers Presented. Speh, J.C. and Moore, R.Y. Retinohypothalamic projections in the macaque monkey. Society for Neuroscience Abstracts. 17:670, 1991.

Inventions, Patents. None.